

*D2*  
In Claim 6, line 6, between "bronchodilation" and "and" insert --while simultaneously reducing undesirable side effects---;

In Claim 9, line 2, delete "an optically pure" and instead insert ---the---.

REMARKS

The instant Application is a continuation of Application Serial No. 07/461,262 ("the parent case").

The above amendments to the Claims have been made to more distinctly claim the subject matter of the invention. Support for these amendments can be found on page 2, line 6-page 3, line 6; page 3, lines 8-14; and page 6, lines 14-27 of the specification. The relationship between these amendments to the Claims and the response to the Office Action of December 9, 1991 in the parent case will be more fully explained below.

Rejection of Claims 1-6, 8, 9, 13 and 14 under 35 U.S.C. §103.

Claims 1-6, 8, 9, 13 and 14 were rejected under 35 U.S.C. §103 over Chemical Abstracts which, as previously stated by the Examiner, teaches salbutamol (albuterol) used to treat asthma and compositions containing albuterol. The case, *In re Adamson et al.*, was cited as teaching that the difference in activity between isomers is not unexpected.

Applicants respectfully submit that the claims, as amended, overcome the rejection. The Chemical Abstracts reference shows the bronchodilation effects of salbutamol and drug combinations incorporating salbutamol. However, this reference does not teach the use of a quantity of the R(-) isomer of albuterol sufficient to cause bronchodilation while simultaneously reducing undesirable side effects associated with racemic albuterol.

Although *In re Adamson et al.* teaches that optical isomers themselves are unpatentable over compounds that the art recognizes as having optical isomers, it is not correct to assume from this that a new method for using an isomer is unpatentable, particularly where, as here, the method unexpectedly provides therapeutic effects without causing undesirable side effects.

One would be led to assume, from the Examiner's apparent interpretation of *In re Adamson et al.*, that the physiological effects of a racemic compound, both therapeutic and adverse, are elicited by the same isomer. However, this assumption is contrary to Applicants' disclosure which teaches that undesirable side effects are associated with the racemic mixture or the therapeutically inactive isomer, i.e. the S(+) isomer, of albuterol, but not with the R(-) isomer. Applicants have, therefore, made the unexpected disclosure that the claimed isomer does not have the same type of activity as the racemic mixture.

Rejection of Claims 1-5 under 35 U.S.C. §103.

Claims 1-5 have been rejected under 35 U.S.C. §103 as being unpatentable over *Brittain et al.*, *Hartley et al.*, *Hawkins et al.*, and *Buckner et al.* who, as previously stated by the Examiner, teach compositions containing the claimed compounds with its isomers used as a bronchodilator in the treatment of asthma and, further, that the R(-) isomer has greater bronchodilation activity over the S(+) isomer.

Applicants respectfully submit that the Claims, as amended, also overcome this rejection. In addition to a complete lack of agreement among the cited references concerning the relative efficacies of the R(-) isomer and the racemate, there is no teaching in these references regarding the administration of a quantity of the R(-) isomer sufficient to effect bronchodilation but without

causing undesirable side effects. The references do not indicate that undesirable side effects can be minimized by administering one of the isomers. Only Applicants' disclosure reveals and claims this important method by administering the R(-) isomer of albuterol.

Rejection of Claims 6, 8, 9, 13 and 14 under 35 U.S.C. §103.

Claims 6, 8, 9, 13 and 14 have been rejected under 35 U.S.C. §103 as being unpatentable over Brittain *et al.*, Hartley *et al.*, Hawkins *et al.* and Buckner *et al.* in view of Chemical Abstracts which, as previously stated by the Examiner, shows combinations of drugs, including salbutamol, used in the treatment of asthma.

Applicants respectfully traverse this rejection, particularly as applied to the presently amended Claims. Although drug combinations including racemic salbutamol are shown in Chemical Abstracts, there is no indication that a combination containing the R(-) isomer minimizes the undesirable side effects associated with the racemic mixture of albuterol. The combination of the other cited references also does not show this element. The combination of drugs which includes the R(-) isomer would not be obvious since undesirable side effects would be expected to be associated with it; there would be no benefit associated with using the R(-) isomer compared with using the racemic mixture. However, Applicants' disclosure shows that undesirable side effects are minimized when the R(-) isomers used. Thus, the combination of drugs including R(-) albuterol is not an obvious extension of a combination of drugs including racemic albuterol.

Rejection of Claims 9, 13 and 14 under 35 U.S.C. §112,  
second paragraph.

Claims 9, 13 and 14 have been rejected under 35 U.S.C. §112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter of the invention. It was stated that Claims 13 and 14 do not have proper antecedent support in Claim 9. Claims 9, 13 and 14 were also rejected as being too broad absent recitation of amounts of ingredients present.

Claim 9 has been presently amended to remove the phrase "optically pure". It is believed that Claims 13 and 14 now have proper antecedent basis and specify the amount of purity of the R(-) isomer of albuterol.

Applicants again respectfully traverse the rejection of Claims 9, 13 and 14 because recitations of amounts of ingredients are dependent on a number of physiological factors which make specification of quantities uncertain until the physiological features are known. It is submitted that skilled artisans, when these features are known, can determine the amounts of ingredients based on these physiological factors.

CONCLUSIONS

With the above amendments and for the above stated reasons, Applicants believe the 35 U.S.C. §§103 and 112, second paragraph rejections have been overcome. Applicants respectfully request reconsideration of the Application and allowance thereof.

If the Examiner feels that a telephone conversation would expedite the prosecution of this Application, he is asked to call Applicant's Agent at (617) 861-6240.

Respectfully submitted,

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